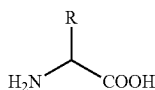


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8. The modified FGF-21 polypeptide of claim 1, wherein said modified FGF-21 polypeptide has an in vivo half-life at least two-fold greater than the human FGF-21 polypeptide of SEQ ID NO: 1.

9. A modified FGF-21 polypeptide comprising a non-naturally encoded amino acid, wherein:

- (a) the modified FGF-21 polypeptide comprises a sequence at least 95% identical to SEQ ID NO: 1 fused to an N-terminal methionine, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5 fused to an N-terminal methionine, SEQ ID NO: 6, or SEQ ID NO: 7;
- (b) the non-naturally encoded amino acid has the structure:



wherein the R group is any substituent other than the side chain found in alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, pyrrolysine, or selenocysteine;

- (c) the modified FGF-21 polypeptide contains a substitution of an amino acid with the non-naturally encoded amino acid at position 108 of SEQ ID NO: 1 or the corresponding amino acid position in SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7;
- (d) the modified FGF-21 polypeptide maintains the biological activity of human FGF-21 polypeptides; and
- (e) the non-naturally encoded amino acid is linked to a linker, polymer, or biologically active molecule.

10. The modified FGF-21 polypeptide of claim 9, wherein the non-naturally encoded amino acid is a phenylalanine derivative or is para-acetyl-L-phenylalanine.

11. The modified FGF-21 polypeptide of claim 9, wherein the non-naturally encoded amino acid comprises a first functional group and the linker, polymer, or biologically active molecule comprises a second functional group, wherein the first functional group and second functional group are not identical and each comprise a carbonyl group, an aminoxy group, a hydrazide group, a hydrazine group, a semicarbazide group, an azide group, or an alkyne group.

12. The modified FGF-21 polypeptide of claim 11, wherein the first functional group on the non-naturally encoded amino acid is a carbonyl moiety and the second functional group on the linker, polymer, or biologically active molecule is an aminoxy moiety, and the resultant covalent linkage created by the reaction of the first and second functional groups is an oxime linkage.

13. The modified FGF-21 polypeptide of claim 9, wherein the polymer comprises a poly(ethylene glycol).

14. The modified FGF-21 polypeptide of claim 13, wherein said poly(ethylene glycol) has an average molecular weight of between about 0.1 kDa and about 100 kDa.

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15. The modified FGF-21 polypeptide of claim 14, wherein said poly(ethylene glycol) has an average molecular weight of about 30 kDa.

16. The modified FGF-21 polypeptide of claim 9, wherein said modified FGF-21 polypeptide has an in vivo half-life at least two-fold greater than the human FGF-21 polypeptide of SEQ ID NO: 1.

17. A modified FGF-21 polypeptide comprising a non-naturally encoded amino acid, wherein:

- (a) said modified FGF-21 polypeptide comprises the polypeptide of SEQ ID NO:1 fused to an N-terminal methionine, except that an amino acid in the modified FGF-21 polypeptide is substituted by a non-naturally encoded amino acid at position 108 of SEQ ID NO: 1;
- (b) said non-naturally encoded amino acid comprises para-acetyl-L-phenylalanine linked to a polymer comprising a poly(ethylene glycol), wherein said poly(ethylene glycol) has an average molecular weight of about 30 kDa; and
- (c) said para-acetyl-L-phenylalanine is linked to said polymer through an oxime linkage.

18. The modified FGF-21 polypeptide of claim 17, wherein said modified FGF-21 polypeptide has an in vivo half-life at least two-fold greater than the human FGF-21 polypeptide of SEQ ID NO: 1.

19. A modified FGF-21 polypeptide comprising a non-naturally encoded amino acid, wherein:

- (a) said modified FGF-21 polypeptide comprises the polypeptide of SEQ ID NO:1 fused to an N-terminal methionine, except that an amino acid in the modified FGF-21 polypeptide is substituted by a non-naturally encoded amino acid at position 108 of SEQ ID NO: 1;
- (b) said non-naturally encoded amino acid comprises para-acetyl-L-phenylalanine linked to a poly(ethylene glycol), wherein said poly(ethylene glycol) has an average molecular weight of about 30 kDa; and
- (c) said para-acetyl-L-phenylalanine is linked to said poly(ethylene glycol) through an oxime linkage.

20. The modified FGF-21 polypeptide of claim 19, wherein said modified FGF-21 polypeptide has an in vivo half-life at least two-fold greater than the human FGF-21 polypeptide of SEQ ID NO: 1.

21. The modified FGF-21 polypeptide of claim 17, wherein said poly(ethylene glycol) comprises a monomethoxy-polyethylene glycol.

22. The modified FGF-21 polypeptide of claim 19, wherein said poly(ethylene glycol) comprises a monomethoxy-polyethylene glycol.

23. The modified FGF-21 polypeptide of claim 17, wherein said poly(ethylene glycol) comprises a linear polyethylene glycol.

24. The modified FGF-21 polypeptide of claim 19, wherein said poly(ethylene glycol) comprises a linear polyethylene glycol.

25. The modified FGF-21 polypeptide of claim 17, wherein said poly(ethylene glycol) comprises a linear monomethoxy-polyethylene glycol.

26. The modified FGF-21 polypeptide of claim 19, wherein said poly(ethylene glycol) comprises a linear monomethoxy-polyethylene glycol.

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